Journal of PeriAnesthesia Nursing xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of PeriAnesthesia Nursing

journal homepage: www.jopan.org

Research

Comparison of the Effect of Massage and EMLA Cream on Children's Physiological Indices During Venipuncture: A Factorial Clinical Trial

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Keywords:
EMLA cream
massage
physiological indices
intravenous line insertion
children

A B S T R A C T

Purpose: The aim of this study was to identify the effect of massage, EMLA cream, and the combination of these two methods on changes in physiological indices because of pain caused by intravenous line insertion in preschool children.
Design: A four-group randomized nonblinded clinical trial with factorial design.
Methods: In total, 140 eligible 3- to 6-year-old children entered the study in Tabriz Children's Hospital in 2017 and were randomly allocated to four groups (EMLA cream, massage, combination of the two, and control). Physiological responses were measured before and immediately after interventions in all groups. Data were collected and analyzed using SPSS version 19.
Findings: Comparison of the physiological indices changes caused by pain between groups showed that changes in children's heart rate (HR) and respiratory rate (RR) in the EMLA group and in the combined-method group were statistically significant ($P < .05$). No significant differences were found in systolic blood pressure and oxygen saturation (SPo_2) between the four groups.
Conclusions: Results indicated that EMLA cream was more effective than massage and a combination of EMLA and massage in reducing an increase in the HR and RR caused by pain in children. Massage alone was not effective in significantly lowering the children's increased physiological indices such as the HR and RR, and it seems the effectiveness of massage is more noticeable in conjunction with EMLA cream.

Pain is a subjective and multifaceted phenomenon, and its impact can potentially lead to unusual physical and mental complications in children.[1,2] Needle-related procedures such as peripheral venous line insertion and application of catheter are considered to be a significant source of pain and anxiety for children in clinical settings.[3-5] Pain associated with such procedures is the source of distress not only for children but also for their parents and the staff implementing these procedures.[6] There is evidence to show that primary painful stimuli have the potential to permanently change the neural pathways that process pain along the spinal cord.[7,8]

Increased heart rate (HR) and respiratory rate (RR), dilated pupils, perspiration, and increased blood pressure are the physiological responses to pain.[1] Pain may also have some psychologically damaging effects on children and their higher functional capabilities.[9,10] Literature has shown that infants and children experiencing a painful procedure are more sensitive to pain, have low-quality cognitive-movement development, give incompatible responses, become afraid of needles, and have traumatic memories that can continue through their teens and adulthood[11,12] and provoke avoidance behavior toward the health care system.[13] Consequently, in recent years, the study of pain management resulting from needle insertion in children has been a noteworthy subject for the health professionals.[14]

Generally, methods of reducing pain are categorized into two main groups: pharmacologic and nonpharmacologic. Pharmacologic methods include using lidocaine 2% cream, tetracaine 4% gel,

Conflict of interest: None to report.

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https://doi.org/10.1016/j.jopan.2020.04.005
1089-9472/

Please cite this article as: Neshat H et al., Comparison of the Effect of Massage and EMLA Cream on Children's Physiological Indices During Venipuncture: A Factorial Clinical Trial, Journal of PeriAnesthesia Nursing, https://doi.org/10.1016/j.jopan.2020.04.005

EMLA cream, nonsteroid and steroid anti-inflammatory drugs, and injectable painkillers.[15] Using topical anesthetic to alleviate pain from needle-related procedures is considered to be the "gold standard" intervention.[13,16] EMLA cream, a mixture of lidocaine 2.5% and prilocaine 2.5%, is a topical anesthetic that blocks the transmission of pain messages to the brain.[17] Several studies have been carried out on the effect of EMLA cream and have reported a significant reduction in pain resulting from different procedures in children of various ages.[18,19] In addition, the effectiveness of this cream has been reported in systematic and meta-analysis reviews.[13] Pain reduction, after applying EMLA cream, not only facilitates implementing procedures but also improves the therapeutic relationship between the patient and personnel.[17,20] However, some of pediatricians and treatment personnel report the delayed anesthetic effect of EMLA cream (30 to 60 minutes)[21-23] as one of the main impediments for using it, particularly in the crowded wards that require prompt actions.[24,25]

In recent years, the use of noninvasive, nonpharmacologic methods have been encouraged as they are economical, do not have side effects, and are independent actions that nurses are able to undertake.[26] Nonpharmacologic methods are classified into two main groups: physical and behavioral. Physical approaches include placing the child in a comfortable position,[27] using a hot or cold compress,[28] massage and dermal stimulations,[29,30] caressing, swaddling, acupuncture, and electrical neural stimulation.[31] Cognitive-behavioral approaches that actively involve the children and help to distract attention from painful procedures include music, the use of a buzzing device, relaxation techniques, watching cartoons, Valsalva maneuver, and using a bubble machine.[26] In a Cochrane review, Wieland[32] reported about the cognitive actions implemented to alleviate pain resulting from needle-related procedures in children and teenagers that mind-occupying techniques (such as watching movies and listening to music), hypnotize, deep breathing techniques, and cognitive-behavioral strategies could help to reduce pain and distress. Ballard et al[33] compared the effects of two methods of pain relief and found that a vibrating device was more effective than the use of topical anesthetic in reducing children's pain during the implementation of needle-related procedures. Among nonpharmacologic interventions, massage has been shown to be effective in controlling pain while also reducing stress and anxiety.[34] Massage blocks the transmission of pain signals through stimulating dermal nerve fibers, and this way, it reduces pain.[35] Several studies have reported massage to be effective in controlling cancer pain and musculoskeletal pains.[28,36,37] Çelebioğlu et al[34] investigated the effect of massage on pain caused by bone marrow biopsy in 25 children in Turkey. The results of this study showed that massage had a positive effect on reducing the acute pain that stemmed from bone marrow biopsy. Similarly, Chik et al[38] used massage for controlling pain caused by cannula insertion in 80 infants in Hong Kong and reported its effectiveness. Aslani et al[39] reported that in 70 children aged 3 to 6 years in Tabriz, HR in children whose hands had been given a massage during venous line insertion, was significantly lower than that of the control group.

Studies show that children are at the risk of physical and physiological side effects such as anxiety in upcoming procedures, reduced pain threshold, and sensitivity to pain; therefore, further research is required to ensure that treatments are available to reduce these potential outcomes.[40,41] The experience of pain in children and teenagers differs with that of adults because some children are unable to describe their pain or cannot understand the reason behind it. Because of children's unique developmental and cognitive levels, communicative skills, and pain experiences, nurses are required to be educated on the proper treatments for pain and support their peers.[26] Although several studies have been conducted worldwide to investigate the effect of pharmacologic and nonpharmacologic methods on pain management in children,[8,42] few studies have investigated the efficacy of the combined methods. The location of this study is the surgery ward of Tabriz Children's Hospital, a referral center for the entire northwest of Iran, where dozens of venous line insertions are performed daily.

This study was carried out to compare three pain management methods, including a pharmacologic method, a nonpharmacologic method, and a combination of the two, during venous line insertion in children aged 3 to 6 years undergoing surgery. This was done with the hope that identification of the effectiveness of one of these methods will inform our pain management strategy.

Materials and Methods

Ethical Considerations

This randomized nonblinded clinical trial used factorial design. The study was registered in the Iran Registry of Clinical Trials (Registration number IRCT20190201042579N1), and approved by the ethics committee of Tabriz University of Medical Sciences. The study setting was the surgery ward of Tabriz Children's Hospital. After a short discussion with the parents, during which an explanation of the study purposes and its implementation was given, informed consent was obtained.

Sample

The sample size was calculated as 30 participants in each group using the following formula with 95% confidence interval, 80% power, and 0.05 accuracy based on the study by Sahiner and Bal,[43] which was conducted to compare three nonpharmacologic methods of reducing pain in children. Taking into account the probability of sample attrition, 15% was added to the figure of 30, and the final number of 35 participants in each group was obtained.

$$n = \frac{\left(z_{1-(\alpha/2)} + z_{1-\beta}\right)^2 \times \left(s_1^2 + s_2^2\right)}{\left(\mu - \mu_2\right)^2} \approx 30$$

$$n = \frac{(1.96 + 0.84)^2 \times \left(0.77^2 + 1.40^2\right)}{(0.40 - 1.23)^2} \approx 30$$

Inclusion criteria included participants aged 3 to 6 years, complete consciousness and physiological stability, no intellectual disability, reduced sensitivity to pain caused by any other disease during the implementation of venous line insertion, no use of analgesia, sedative, corticosteroid, or relaxants. Exclusion criteria included failure in inserting venous line at the first attempt and noncooperative child during the implementation of interventions. Convenience sampling was undertaken. To recruit participants, the researcher visited the surgery ward at the end of the morning work shifts and selected those eligible children who were candidates for surgery the next day and required a venous line.

Randomization and Blinding

To randomly allocate the children to the groups, each of the groups' name (intervention 1, intervention 2, intervention 3 [combined], and control) was written on 35 sheets of paper and these were placed inside identical opaque envelopes. When a

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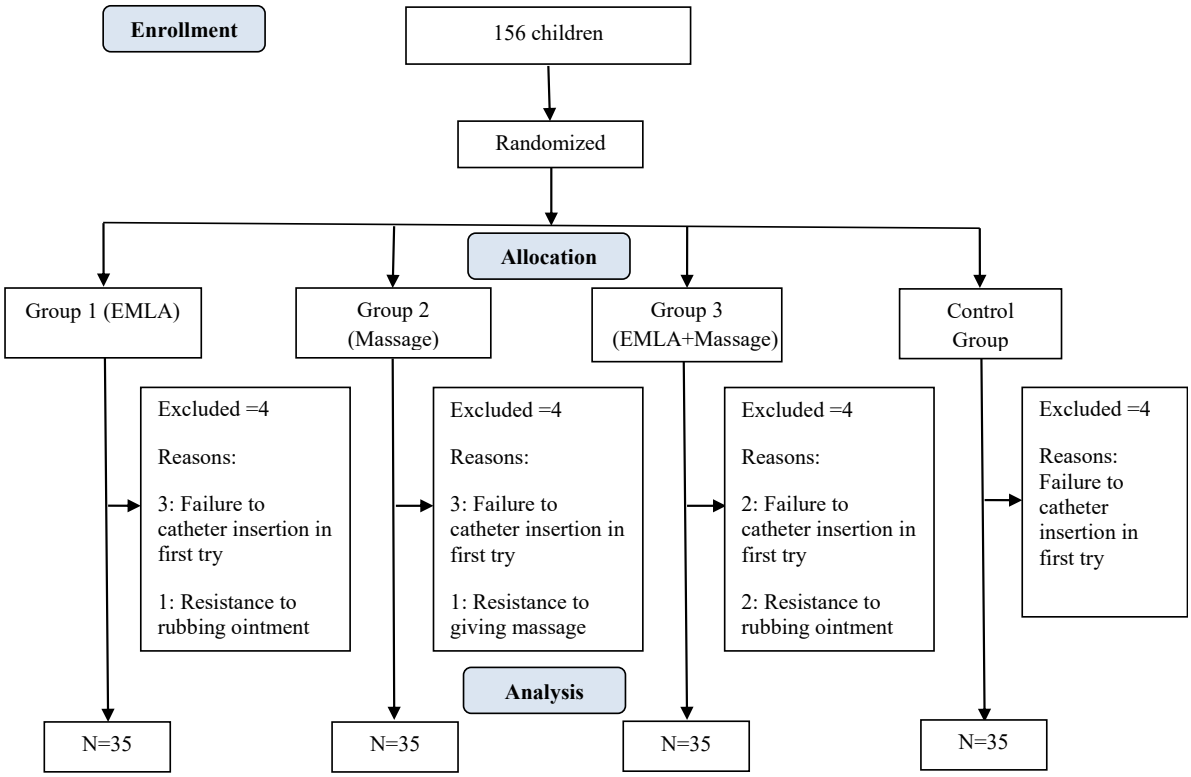

Figure 1. Trial flow chart of eligible participants in the intervention group and the control group. This image is available in color online at www.jopan.org.

participant entered the study, one of the envelopes was opened, and the participant was allocated to that group.

Procedures

An experienced nurse undertook the procedure using an Angiokit no. 22 made by Biçakcilar.com. The dorsal vessels were used, and the cannula was inserted into the child's nondominant hand in the presence of his or her mother and on the bed specified for venipuncture. In intervention group 1, 60 minutes before venous line insertion, 1.5 g EMLA cream (each gram containing 25 mg lidocaine and 25 mg prilocaine) was applied to the insertion area (about 4 cm^2 of the skin), and a dressing covered it. After 60 minutes, the dressing was removed and the area was cleaned, and the venous line was inserted. In intervention group 2, about 5 minutes before starting the intervention and also during the intervention, the researcher massaged the hand and arm where the venous line was being inserted and used moderate palm pushes and gentle strokes around that area. After that an experienced colleague inserted the cannula on the first attempt. In intervention group 3, both massage and EMLA cream were used before the venous line was inserted. In the control group, venous line insertion was implemented routinely. To record the data, a two-section data collection form was used. In the first section, children's demographic information was recorded after being extracted from their medical documents.

Measures

Two nurses with similar work experience (more than 5 years) in the study setting recorded the HR, RR, systolic blood pressure (SBP), and percentage of arterial blood oxygen saturation before and immediately after venous line insertion. A calibrated pulse oximetry model Novametrix was used to measure the HR and oxygen saturation. To measure the blood pressure, a sphygmomanometer model FMT and a pediatric cuff were used. The RR was also observed meticulously for 1 minute and recorded. To be assured of the reliability between the two nurses' observations of blood pressure and RR, the first 10 measures collected by both nurses were compared, Cohen's kappa coefficient was calculated and coefficient of 0.9 was achieved.

Statistical Analysis

To analyze the data, SPSS software version 19 and the descriptive statistics, paired *t* test, one-way analysis of variance, and Tukey HSD post hoc tests were used. The *P* value <.05 was considered as significant in all tests.

Table 1
Characteristics of Children in Intervention and Control Groups

Variable	Group 1 (EMLA)	Group 2 (Massage)	Group 3 (EMLA + Massage)	Control Group	*f*	*P**
Mean of age (y)	1.15 ± 4.58	1.08 ± 4.54	0.94 ± 4.48	1.04 ± 4.40	0.2	.89
Mean of weight (kg)	4.24 ± 17.65	3.77 ± 17.18	3.08 ± 16.88	3.17 ± 16.64	0.51	.67

* One-way analysis of variance.

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Table 2
Physiological Indices Before and After Venipuncture in Intervention and Control Groups

Variable	Group 1 (EMLA)		Group 2 (Massage)		Group 3 (EMLA + Massage)		Control Group	
	Before	After	Before	After	Before	After	Before	After
RR	26.97 ± 17.47 $t = -2.38$ $P = .02$*	27.74 ± 18.09	24.06 ± 2.65 $t = -5.51$ $P = .00$	25.63 ± 2.91	30.63 ± 24.26 $t = -3.09$ $P = .00$	31.97 ± 25.20	24.71 ± 2.37 $t = -5.89$ $P = .00$	27.00 ± 3.14
HR	113.60 ± 17.98 $t = -3.79$ $P = .00$	116.7 ± 19.3	118.43 ± 7.46 $t = -4.66$ $P = .00$	122.37 ± 7.85	109.11 ± 27.54 $t = -5.24$ $P = .00$	112.11 ± 28.38	119.57 ± 8.12 $t = -4.10$ $P = .00$	126.74 ± 6.07
SBP	94.29 ± 7.48 $t = -0.68$ $P = .49$	94.60 ± 7.89	93.58 ± 5.63 $t = -2.65$ $P = .01$	94.43 ± 5.39	90.86 ± 6.00 $t = 0.00$ $P = 1$	90.86 ± 5.48	92.14 ± 6.09 $t = -1.78$ $P = .08$	93.00 ± 5.58
SPo_2	94.17 ± 2.17 $t = -2.26$ $P = .03$	94.71 ± 1.70	93.77 ± 1.49 $t = -4.19$ $P = .00$	94.54 ± 1.54	93.11 ± 1.43 $t = -4.27$ $P = .00$	93.91 ± 1.40	95.74 ± 1.70 $t = -3.35$ $P = .00$	96.54 ± 1.94

HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; SPo_2, peripheral capillary oxygen saturation.
* Paired *t* test.

Results

Demographic and Clinical Variables

In total, 156 eligible children entered the study. Among these, 16 children were excluded from the study because of reasons such as failure in venous line insertion at the first attempt (12 children), lack of cooperation during applying EMLA cream (3 children), and resistance from receiving massage (1 child). Participants were randomly allocated to four groups of EMLA cream, massage, massage and EMLA cream, and control group. Ultimately, the data collected from 140 children (35 participants in each group) were analyzed (Figure 1). Of all participants, 87 (62.1%) were male and 53 (37.9%) were female. Statistically, there was no significant difference between participants' personal and demographic information in all four groups. Their gender and mean age and weight are shown separately in Table 1.

Main Outcomes

A total of 165 children's physiological indices were compared within the intervention and control groups before and after venous line insertion. The results of the data analysis showed that there was a significant difference in physiological indices before and after venous line insertion in the intervention groups. However, changes in SBP in intervention group 1 (EMLA cream) and intervention group 3 (EMLA cream and massage) were not significant before and after venous line insertion. Table 2 shows the statistical analysis of the changes in physiological indices in all groups.

Comparison of the changes in physiological indices between intervention and control groups indicated that of four physiological indices, changes in RR were statistically significant between groups. Changes in SBP and peripheral capillary oxygen saturation (SPo_2) were not significant (Table 3).

Pairwise comparison of the groups using Tukey HSD post hoc test showed that in intervention group 1 (EMLA cream) compared with the control group, changes in the HR and RR were significant. In addition, in intervention group 3 (EMLA cream and massage) compared with the control group, changes were significant only in the HR (Table 4).

Discussion

This study aimed to compare the effectiveness of massage and EMLA cream, as nonpharmacologic and pharmacologic methods, respectively, when used alone and in combination with each other, on the changes in physiological indices (HR, RR, SBP, and SPo_2) after venous line insertion in children aged 3 to 6 years old candidate for surgery.

Changes in the HR in intervention 1 (EMLA cream) and intervention 3 (EMLA cream and massage) were statistically significant compared with other groups. In intervention group 3 (EMLA cream and massage), this significance was more considerable. Massage alone did not have a significant effect on reducing an increase in the HR caused by pain and the measures were not maintained as favorable compared with the control group. However, its effectiveness was intensified when used in conjunction with EMLA cream. Ackerman et al[44] investigated the effect of massage on pain in children having cell transplantation using a qualitative analysis of open-ended interviews with the parents and practitioners. Their study results showed that massage reduced the symptoms associated with cell transplantation and promoted children's sleep and relaxation. O'Flaherty et al[45] reported similar results on the positive effect of massage on significantly reducing the HR and RR of children with burns. In contrast, in the study by Staveski et al[46] and Van Dijk et al,[42] massage did not have a significant effect on reducing children's HR resulting from pain caused by a burn and a surgery. However, Aslani et al[39] found that hand massage during venous line insertion significantly lowered children's HR. Basiouny and Hamed[47] investigated the effect of skin mechanical stimulation on pain resulting from venipuncture in children suffering from leukemia. They reported that thermomechanical stimulation was

Table 3
Differences of Physiological Indices' Mean Before and After Venipuncture Between Intervention and Control Groups

Groups Changes	Group 1 (EMLA)	Group 2 (Massage)	Group 3 (EMLA + Massage)	Control Group	*f*	*P**
RR	0.77 ± 1.91	1.57 ± 1.68	1.34 ± 2.56	2.28 ± 2.29	2.99	.03
HR	3.11 ± 4.86	3.94 ± 5.00	3.00 ± 3.38	7.17 ± 10.32	3.20	.02
SBP	0.31 ± 2.69	0.85 ± 1.91	0.00 ± 2.10	0.85 ± 2.84	1.07	.36
SPo_2	0.54 ± 1.42	0.77 ± 1.08	0.80 ± 1.10	0.80 ± 1.41	0.33	.79

HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; SPo_2, peripheral capillary oxygen saturation.
* One-way analysis of variance.

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Table 4
Significance of HR and RR Changes in Groups' Pairwise Comparison

Group	Comparison Groups	Changes In	P*	Group	Comparison Groups	Changes In	P
EMLA	Massage	RR	.403	Massage	EMLA + massage	RR	.097
		HR	.950			HR	.092
	EMLA + massage	RR	.680		Control	RR	.505
		HR	1.000			HR	.161
	Control	RR	.019	EMLA + massage	Control	RR	.258
		HR	.047			HR	.038

HR, heart rate; RR, respiratory rate.
* Tukey HSD.

effective in reducing physiological and behavioral pain responses during and after venipuncture among children with leukemia. The observed differences among these studies could be because of the discrepancies in study designs and children's condition.

A further finding in our study was that change in the RR was only significant in intervention group 1 (EMLA cream), that is, EMLA cream outperformed massage and the combined method in reducing the RR resulting from pain caused by venous line insertion. In several studies, it has been shown that applying EMLA cream on the insertion area reduces children's pain and stress significantly.[17,29,48] Akdas et al[49] conducted a study in which the effect of EMLA cream and Valsalva maneuver on pain associated with venipuncture was compared. They reported that EMLA cream reduced children's pain significantly compared with Valsalva maneuver and the changes in their HR and mean arterial pressure after intervention were statistically significant in the EMLA cream group. The results of that study, which are consistent with the present study, showed that although nonpharmacologic methods of pain management were more accessible and inexpensive, they could not be considered as an appropriate alternative for EMLA cream.

In our study, none of the interventions had a significant effect on SBP and SPo_2. Similarly, in the study by Ahn et al,[18] EMLA cream did not change the children's SPo_2 significantly. Nevertheless, Fooladi et al[50] and Kunjumon and Upendrababu[51] used mind-occupying methods during the implementation of needle-related procedures and found it could change children's hemodynamic parameters significantly. In our study, the combination of EMLA cream and massage reduced children's HR during venous line insertion. Therefore, it seems that combining EMLA cream with massage increases the effectiveness of these methods in controlling the physiological indices changes induced by pain.

Limitations

Each individual's pain perception responses to pain and sensitivity to touch are considered as limitations of the present study. Overcrowding and loud noises that could also cause distress were beyond the researcher's control. The authors suggest that further studies should be conducted in a more controlled setting in terms of interfering noises.

Conclusions

According to the results of this study, EMLA cream was more effective than massage and a combination of EMLA and massage in reducing an increase in the HR and RR after venous line insertion in children aged 3 to 6 years. Although nonpharmacologic pain management methods are more accessible and inexpensive, they cannot be considered as an appropriate alternative to EMLA cream in controlling physiological changes induced by pain. In this study, massage alone did not have a significant effect on reducing the changes in children's physiological indices. However, its effectiveness increased in combination with EMLA cream. Consequently, it seems that through combining massage with EMLA cream, the effectiveness of it in reducing children's increased HR resulting from pain can be intensified.

Acknowledgments

The authors would like to appreciate Dr Wendy Higman from Coventry University for gratefully providing linguistic and content comments on this article. They also express their sincere gratitude to all children, their parents, and the surgery ward personnel for their kind cooperation. This study was exclusively approved and sponsored by Tabriz University of Medical Sciences, Tabriz, Iran (grant number: IR.TBZMED.REC.1395.134).

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Please cite this article as: Neshat H et al., Comparison of the Effect of Massage and EMLA Cream on Children's Physiological Indices During Venipuncture: A Factorial Clinical Trial, Journal of PeriAnesthesia Nursing, https://doi.org/10.1016/j.jopan.2020.04.005